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Research Article

Effects of Serum Creatinine on Heart, Diabetes, and Anaemia Patients

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Abstract

Objectives: The report aims to examine the effects of serum creatinine (SCT) on heart, diabetes, anaemia and normal study units, and along with the other biological factors. The study is based on the relationship of serum creatinine with heart, diabetes, anaemia patients and many other factors.

Materials & Methods: A real data set of 299 heart patients with 13 study characters is taken in the current study, the data set is available herein: https://archive.ics.uci.edu/ml/datasets/Heart+failure+clinical+records, and the serum creatinine probabilistic model has been developed applying statistical joint generalized linear models.

Results: From the fitted Log-normal model, the mean serum creatinine (SCT) is positively associated with age (P<0.0001). It is partially negatively associated with ejection fraction (EFT) (P=0.0974) and partially positively associated with the joint interaction effects (JIEs) of EFT and the death-event (DEE), i.e., EFT*DEE (P=0.1168). It is negatively associated with creatinine phosphokinase (CPK) (P<0.0001) and serum sodium (SNa) (P<0.0001), while it is positively associated with their JIEs, i.e., CPK*SNa (P<0.0001). It is negatively associated with high blood pressure (BP) (P=0.0030). It is partially negatively associated with the JIEs of anaemia status (ANS) and time up to the end of the follow-up period (TFP) i.e., ANS*TFP (P=0.1299), while it is independent of both the ANS and TFP. It is negatively associated with the smoking status (SMS) (P=0.0007), and positively associated with the JIEs of SMS and TFP, i.e. SMS*TFP (P=0.0016). Variance of SCT is negative associated with age (P=0.0543) and ANS (P=0.0044), while it is positively associated with their JIEs, i.e. AGE*ANS (P=0.0070). SCT variance is negatively associated with CPK (P=0.0001), while it is partially positively associated with the JIEs of CPK and ANS i.e., CPK*ANS (P=0.1482). Variance of SCT is negatively associated with diabetes mellitus status (DMS) (P=0.0199), while it is positively associated with the JIEs of CPK and DMS i.e., CPK*DMS (P=0.0086). There are many more significant effects in the SCT variance model.

Conclusions: From this data set, it is clear that mean and variance of serum creatinine is associated with the heart, diabetes and anaemia patients. It affects age, EFT, CPK, SNa, PLC, BP, ANS, DMS, SMS, SEX, TFP, DEE and their many joint interaction effects.

Key words: creatinine phosphokinase (CPK); ejection fraction (EFT); hypertension; joint generalized linear models (JGLMs); serum creatinine (SCT); serum sodium (SNa)

Introduction

Several studies pointed out that elevated serum creatinine (SCT) may be an independent explanatory factor of all-cause of cardiovascular disease parameters and mortality predictor variables [1-4]. These articles have studied some specific cardiac disease groups such as patients with recent stroke [1], hypertensive individuals [2], survivors of myocardial infarction [3], and the elderly individuals [4]. Effects of SCT level on hypertension have been studied in different articles [5-8], but there is no firm conclusion of the effect of SCT on high blood pressure (BP). Some articles have tried to identify the effects of SCT on some other cardiac parameters such as ejection fraction (EFT), heart rate, BP and stroke, but there are no definite conclusions [5-8].

Role of SCT on diabetes patients has been studied in different articles [9-13]. A very few articles have focused on association of low SCT level with type 2 diabetes mellitus [14-16]. For example, a case-control study of 1122 study units in Trinidad and Tobago showed an association of low

SCT level with type 2 diabetes mellitus [14]. Similarly, a cross-sectional study of 1017 subjects with morbid obesity age group 18–75 years have shown a positive association between SCT level and diabetes prevalence [15]. Article [16] has studied whether low SCT level, a surrogate marker of skeletal muscle mass, was correlated with an increased risk of incident dysglycemia including type 2 diabetes mellitus.

Effects of SCT levels on anaemia patients have been studied in different articles [17-20]. Previous articles have tried to establish a relationship between hemoglobin (Hgb) levels and SCT levels of anaemia patients. Numasawa, Inohara, Ishii et al. [17] have tried to derive a simple composite indicator of baseline Hgb and SCT levels to examine their joint (or compound) effects on clinical outcomes. These researchers have derived a single explanatory factor (or index) namely Hgb/SCT ratio to examine the effects of clinical outcomes. Earlier articles [18-20] have pointed out that preprocedural anemia and impaired renal function are correlated with each other. It is observed that there is no definite conclusion based on some suitable statistical modeling. These findings may invite some doubts and debates.

Some earlier articles have examined the effects of serum creatinine (SCT) on heart, diabetes and anaemia patients using simple correlation, regression analysis, and machine learning etc. Most of the earlier articles invite some doubts and debates, as the analysis approaches that are used in the earlier articles are not appropriate. In addition, appropriate model diagnostics of the used methods are not discussed in the earlier articles. The effects of SCT are little studied based on probabilistic modelling. The current article examines the following research queries.

- Is there any association of serum creatinine with heart, diabetes and anaemia patients along with other biochemical factors? If it is affirmative, what is the most probable serum creatinine association model?
- How do we derive the most probable serum creatinine association model?
- What are the roles of serum creatinine on the heart, diabetes and anaemia patients along with other biochemical factors?

The article searches the above research problems considering the following sections such as materials & methods, statistical analysis & results, discussions, and conclusions. The serum creatinine probabilistic model is displayed in Table 1 based on the data set pointed in the materials section. The probabilistic serum creatinine means and dispersion models are developed by joint generalized linear models (JGLMs), which is described in the methods section. The obtained findings of SCT analysis are presented in the results section, and the results are illustrated in the discussion section. Based on the derived SCT probabilistic model, the present article has obtained some information that is presented in the conclusions section.

Material & Statistical Methods

Materials

The serum creatinine probabilistic model is derived herein using a data set of 299 heart failure subjects collected from the Faisalabad Institute of Cardiology under the Allied Hospital at Faisalabad in Punjab, Pakistan, during the period April to December 2015 [21, 22]. The data set is available in the site

https://archive.ics.uci.edu/ml/datasets/Heart+failure+clinical+records,

The data set is clearly presented by the authors in the article [22]. The original study [21] contained 194 male and 105 female subjects, and they all had left ventricular systolic dysfunction. All the subjects had previous heart failures, and accordingly, they were classed in III or IV heart failure stages of New York Heart Association (NYHA) classification [23]. The ethics approval and the participant consents of the study is clearly stated in the original article [21]. Recently an article by Chicco and Jurman [24] illustrates clearly this heart failure data set using two tables, which describe separately continuous and attribute characters.

The study contains 13 characters out of which 7 are continuous and 6 are attribute. The continuous study characters are age (x1), creatinine phosphokinase (CPK) (x3), ejection fraction (EFT) (x5), platelets count (PLC) (x7), serum creatinine (SCT) (x8), serum sodium (SNa) (x9), time up to the end of the follow-up period (TFP) (x12), while the attribute characters are anaemia status (ANS) of the patients (0= no anaemia, 1= anaemia) (Fx2), diabetes mellitus status (DMS) of the patients (0= no diabetes, 1= diabetes) (Fx4), high blood pressure (BP) of patients (0= normal BP, 1=high BP) (Fx6), sex (0=female, 1=male) (Fx10), smoking status (SMS) (0=no smoking, 1= smoking) (Fx11), death event (DEE) (0=alive, 1=death) (Fx13). A subject was classed as anaemia patient if his/her haematocrit levels were lower than 36% [21]. There is no information regarding the classification of high BP patients in the original article [21]. The death event indicates that the patient died (=1) or survived (=0) up to the end of the follow-up period, that was 130 days on average [21].

The creatinine phosphokinase (CPK) indicates the CPK enzyme levels in blood. If a muscle tissue gets damaged, CPK flows into the blood. So high CPK enzyme levels in the blood of a subject might indicate a heart failure or injury [25]. The serum creatinine (SCT) is a waste product produced by creatine, if a muscle breaks down. High serum creatinine levels in blood may indicate renal dysfunction [26]. Medical practitioners focus on serum creatinine in blood to examine the kidney function [27]. The original data source article [21] unfortunately does not present any information whether any patient had primary kidney disease or not, and it does not provide any additional information about what type of follow-up was carried out for examining kidney disease patients. The ejection fraction (EFT) indicates the percentage of how much blood the left ventricle pumps out with each contraction. Serum sodium (SNa) a mineral substance is responsible for the correct functioning of nerves and muscles. The serum sodium blood routine test of a subject indicates the normal or abnormal levels of sodium in the blood. An abnormally low level of sodium in the blood might be caused by heart failure [28]. Further information about the data set can be obtained easily from the original articles [21, 22]. Interested readers may go through the original articles [21, 22].

Statistical Methods

In the present study, serum creatinine (SCT) is the aimed response random variable that is to be modeled with the left biochemical, cardiac, disease status and physiological factors. It is identified that the response SCT is heteroscedastic and non-normally distributed random variable. The variance of SCT is not stabilized with any suitable transformation, so it is modeled herein using joint generalized linear models (JGLMs) under both the gamma and log-normal distribution, which has been clearly given in [29-32]. For detailed discussion about JGLMs, interested readers may consult with the book by Lee, Nelder and Pawitan [29]. Very shortly JGLMS under both the gamma and log-normal distribution are shortly presented herein.

JGLMs for log-normal distribution: For the positive response Y_i (=SCT) with $E(Y_i=SCT) = \mu_i$ (mean) and $Var(Y_i=SCT) = \sigma_i^2 \mu_i^2 = \sigma_i^2 V(\mu_i)$ say, where σ_i^2's are dispersion parameters, and $V(\cdot)$ reveals the variance function. Generally, the log transformation $Z_i = \log(Y_i=SCT)$ is applied to stabilize the variance $Var(Z_i) \approx \sigma_i^2$, but the variance may not always be stabilized [32]. For developing an improved model, JGLMs for the mean and dispersion are considered. For the response SCT, assuming log-normal distribution, JGL mean and dispersion models (with $Z_i = \log(Y_i=SCT)$) are as follows:

$E(Z_i) = \mu_{zi}$ and $Var(Z_i) = \sigma_{zi}^2$,

$\mu_{zi} = x_i^t \beta$ and $\log(\sigma_{zi}^2) = g_i^t \gamma$,

where x_i^t and g_i^t are the dependent or explanatory factors/variables vectors linked to the regression coefficients β and γ, respectively.

JGLMs for gamma distribution: For the above stated Y_i's (=SCT), the variance has two components such as $V(\mu_i)$ (based on the mean parameters) and σ_i^2 (free of μ_i's). The variance function $V(\cdot)$ reveals the GLM family distributions. For example, if $V(\mu) = \mu$, it is Poisson, gamma if $V(\mu) = \mu^2$, and normal if $V(\mu) = 1$ etc. Gamma JGLMs means and dispersion models of SCT are as follows:

$$\eta_i = g(\mu_i) = x_i^t \beta \text{ and } \varepsilon_i = h(\sigma_i^2) = w_i^t \gamma,$$

where $g(\cdot)$ and $h(\cdot)$ are the GLM link functions associated for the mean and dispersion linear predictors respectively, and x_i^t, w_i^t are the explanatory factors/variables vectors attached with the mean and dispersion parameters respectively. Maximum likelihood (ML) method is used for estimating mean parameters, while the restricted ML (REML) method is applied for estimating dispersion parameters, which are explicitly stated in the book by Lee, Nelder and Pawitan [29].

Statistical Analysis & Results

Statistical Analysis

The response SCT is modeled by JGLMs with both the Gamma and Log-normal distributions. In the analysis, SCT is considered as the response (dependent) variable, and the remaining 12 variables are considered as the SCT's explanatory variables. Final model has been chosen based on the lowest Akaike information criterion (AIC) value (within each class), which minimizes both the squared error loss and predicted additive errors [33, p. 203--204]. According to the AIC criterion, JGLMs Log-normal fit (AIC=**301.0**) is better than the Gamma fit (AIC= **345.513**).

In the SCT mean model, only one main effects sex (=Fx10) (P=0.2478) (insignificant in the Log-normal model, while it is partially significant in the Gamma model (P=0.1234)), and two partially significant joint effects such as EFT*DEE (x5*Fx13) (P=0.1168) and TFP*ANS (x12*Fx2) (P=0.1299) are included for better model fitting [33]. Note that in Epidemiology, partial significant effects are known as confounders. The other partially or insignificant effects such as EFT (x5) (P=0.0974), DEE (Fx13) (P=0.7184), TFP (x12) (P=0.3731) and ANS (Fx2) (P=0.4901) are included in the mean model due to Nelder's marginality rule [34], namely that if an interaction effect (for example, here EFT*DEE) is significant or partially significant, so all its related lower-order effects (for example, here EFT and DEE) should be included in the mean model. Similarly, in the variance model, some partially significant or insignificant effects such as CPK*ANS (x3*Fx2) (P=0.1482), TFP*ANS (x12*Fx2) (P=0.2757) (for Gamma model (P=0.1482)) and SMS (Fx11) (P=0.3812) are included. In both the fitted models there are many discrepancies such as AIC values, values of the estimates, standard errors, P-values etc. [34]. Log-normal fitted models give better fit, and the analysis results are presented for both the models in Table 1.

The derived SCT's probabilistic model (Table 1) is a data derived model that should be examined using model checking tools. All the valid interpretations are drawn from the data generated probabilistic model. For the joint Log-normal fitted SCT models (Table 1), model verification graphical analysis is displayed in Figure 1. Figure 1(a) presents the SCT fitted absolute residuals against the fitted values, which is almost a flat line, implying that variance is constant with the running means. Figure 1(b) displays the normal probability plot for the SCT fitted mean model (Table 1) that does not show any lack of fit. These two Figures 1(a) and 1(b) do not show any SCT fitted model's (Table 1) discrepancy. These two figures show that the Log-normal fitted SCT model (Table 1) is an approximate of the unknown SCT model.

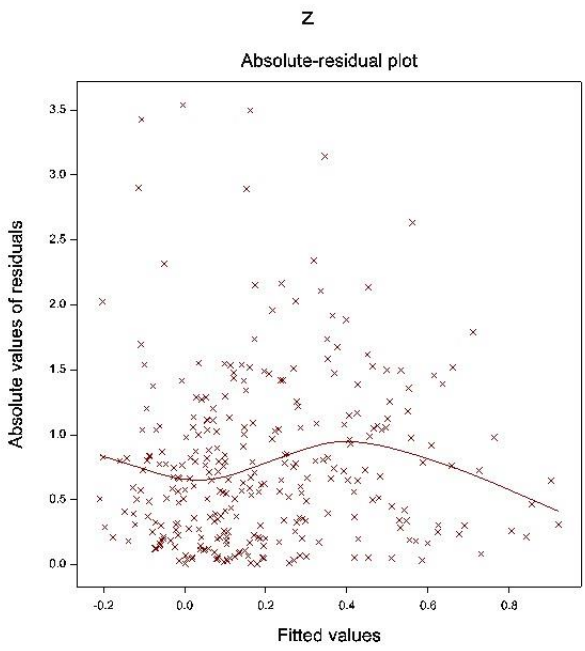

Figure. 1 (a)

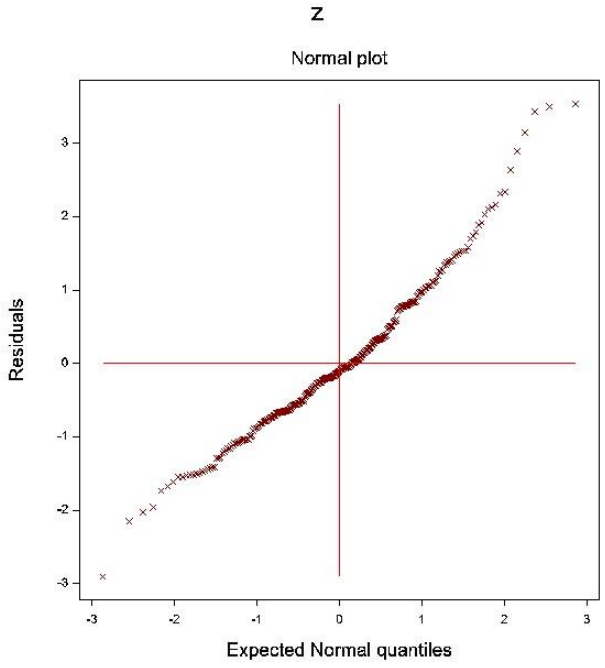

Figure 1 (b)

Figure 1: For the joint Log-normal SCT fitted models (Table 1), the (a) absolute residuals plot with the SCT fitted values, and (b) the normal probability plot for the SCT mean model

Results

Final SCT analysis outcomes for both the fitted Log-normal and Gamma models are displayed in Table 1. AIC rule selects the Log-normal fitted SCT model. The following results are described herein using the SCT fitted Log-normal model.

From the SCT fitted mean Log-normal model (Table 1), it is derived that mean SCT is positively associated with AGE (P<0.0001). It is partially negatively associated with ejection fraction (EFT) (P=0.0974) and partially positively associated with the joint interaction effects (JIEs) of EFT*DEE (P=0.1168). It is negatively associated with creatinine phosphokinase (CPK) (P<0.0001) and serum sodium (SNa) (P<0.0001), while it is positively associated with their JIEs, i.e., CPK*SNa (P<0.0001). It is negatively associated with high blood pressure (BP) (P=0.0030). It is partially negatively associated with the JIEs of anaemia status (ANS) and time up to the end of the follow-up period (TFP) i.e., ANS*TFP (P=0.1299), while it is independent of both the ANS (P=0.4901) and TFP (P=0.3731). Mean SCT is negatively associated with the smoking status (SMS) (P=0.0007), and positively associated with the JIEs of SMS and TFP, i.e. SMS*TFP (P=0.0016).

From the SCT fitted dispersion Log-normal model (Table 1), it is derived that the variance of SCT is negatively associated with age (P=0.0543) and ANS (P=0.0044), while it is positively associated with their JIEs, i.e. AGE*ANS (P=0.0070). SCT variance is negatively associated with CPK (P=0.0001), while it is partially positively associated with the JIEs of CPK and ANS i.e., CPK*ANS (P=0.1482). Variance of SCT is negatively associated with diabetes mellitus status (DMS) (P=0.0199) and CPK (P=0.0001), while it is positively associated with their JIEs of CPK*DMS (P=0.0086). SCT variance is negatively associated with EFT (P=0.0019) and ANS (P=0.0044), while it is positively associated with their JIEs of EFT*ANS (P=0.0234). It is negatively associated with PLC (P=0.0547) and BP (P=0.0137), while it is positively associated with their JIEs of PLC*BP (P=0.0347). It is negatively associated with DEE (P=0.0002) and EFT (P=0.0019), while it is positively associated with their JIEs of EFT*DEE (P<0.0001). It is negatively associated with TFP (P=0.1416) (partially) and ANS (P=0.0044), while it is partially negatively associated with their JIEs of EFT*DEE (P=0.2757). Variance of SCT is partially positively associated SEX (P=0.0914), while it is indifferent to SMS (P=0.3812).

Log-normal fitted SCT mean ($\hat{\mu}_z$) model (Table 1) is

$\hat{\mu}_z$= 2.83 + 0.007 AGE – 00029 EFT + 0.0519 DEE + 0.0069 EFT*DEE – 0.0019 CPK – 0.0215 SNa + 0.0001 CPK*SNa – 0.1113 BP – 0.0003 TFP + 0.0602 ANS – 0.0008 TFP*ANS + 0.049 SEX – 0.2591 SMS + 0.0015 TFP*SMS,

and the fitted SCT variance ($\hat{\sigma}^2_z$) model is

$\hat{\sigma}^2_z$= exp. (1.6286 – 0.0224 AGE – 4.0776 ANS + 0.0518 AGE*ANS - 0.0006 CPK + 0.0005 CPK*ANS – 0.5959 DMS + 0.0006 CPK*DMS – 0.0355 EFT + 0.0332 EFT*ANS – 0.0001 PLC – 1.4723 BP + 0.0001 PLC*BP–2.4493 DEE + 0.0767 EFT*DEE– 0.0028TFP – 0.0032 TFP*ANS + 0.4080 SEX – 0.2012 SMS).

Note that mean SCT is explained by AGE, EFT, DEE, EFT*DEE, CPK, SNa, CPK*SNa, BP, TFP, ANS, TFP*ANS, SEX, SMS, TFP*SMS, while its variance is explained by AGE, ANS, AGE*ANS, CPK, CPK*ANS, DMS, CPK*DMS, EFT, EFT*ANS, PLC, BP, PLC*BP, DEE, EFT*DEE, TFP, TFP*ANS, SEX, SMS.

Model	Covariates	Gamma Model Fit				Log-Normal Model Fit			
		Estimate	s.e.	t-value	p-value	Estimate	s.e.	t-value	p-value
Mean	constant	3.1105	0.6709	4.636	<0.0001	2.8300	0.6385	4.432	<0.0001
	AGE (x1)	0.0072	0.0016	4.472	<0.0001	0.0070	0.0015	4.497	<0.0001
	EFT (x5)	-0.0037	0.0018	-2.008	0.0456	-0.0029	0.0017	-1.663	0.0974
	DEE(Fx13)	-0.1619	0.1516	-1.068	0.2864	0.0519	0.1437	0.361	0.7184
	x5*Fx13	0.0139	0.0046	2.956	0.0034	0.0069	0.0044	1.573	0.1168
	CPK(x3)	-0.0021	0.0004	-4.940	<0.0001	-0.0019	0.0004	-4.403	<0.0001
	SNa (x9)	-0.0230	0.0049	-4.662	<0.0001	-0.0215	0.0046	-4.585	<0.0001
	x3*x9	0.0001	0.0001	4.773	<0.0001	0.0001	0.0001	4.273	<0.0001
	BP (Fx6)	-0.1222	0.0401	-3.051	0.0025	-0.1113	0.0373	-2.988	0.0030
	TFP (x12)	-0.0004	0.0004	-1.075	0.2833	-0.0003	0.0003	-0.892	0.3731
	ANS(Fx2)	0.1491	0.0922	1.618	0.1068	0.0602	0.0870	0.691	0.4901
	x12*Fx2	-0.0013	0.0005	-2.466	0.0142	-0.0008	0.0005	-1.519	0.1299
	SEX(Fx10)	0.0696	0.0451	1.545	0.1234	0.0490	0.0423	1.158	0.2478
	SMS(Fx11)	-0.2570	0.0765	-3.358	0.0009	-0.2591	0.0758	-3.417	0.0007
	x12*Fx11	0.0014	0.0005	2.965	0.0033	0.0015	0.0005	3.191	0.0016
Dispersion	Constant	1.6712	1.1746	1.423	0.1558	1.6286	1.1068	1.472	0.1421
	AGE(x1)	-0.0184	0.0122	-1.510	0.1321	-0.0224	0.0116	-1.932	0.0543
	ANS(Fx2)	-3.6705	1.4494	-2.532	0.0119	-4.0776	1.4191	-2.873	0.0044
	x1*Fx2	0.0431	0.0194	2.216	0.0275	0.0518	0.0191	2.716	0.0070
	CPK(x3)	-0.0006	0.0002	-4.182	<0.0001	-0.0006	0.0002	-3.889	0.0001
	x3*Fx2	0.0007	0.0004	1.696	0.0910	0.0005	0.0004	1.450	0.1482
	DMS(Fx4)	-0.6130	0.2659	-2.305	0.0219	-0.5959	0.2545	-2.341	0.0199
	x3*Fx4	0.0007	0.0003	2.594	0.0100	0.0006	0.0002	2.644	0.0086
	EFT (x5)	-0.0393	0.0116	-3.404	0.0007	-0.0355	0.0113	-3.126	0.0019
	x5*Fx2	0.0387	0.0149	2.593	0.0100	0.0332	0.0146	2.279	0.0234
	PLC(x7)	-0.0001	0.0001	-1.988	0.0478	-0.0001	0.0001	-1.929	0.0547
	BP(Fx6)	-1.2327	0.6029	-2.045	0.0418	-1.4723	0.5938	-2.480	0.0137
	x7*Fx6	0.0001	0.0001	1.870	0.0625	0.0001	0.0001	2.122	0.0347
	DEE(Fx13)	-2.6839	0.6671	-4.023	<0.0001	-2.4493	0.6584	-3.720	0.0002

	x5*Fx13	0.0813	0.0165	4.938	<0.0001	0.0767	0.0160	4.791	<0.0001
	TFP(x12)	-0.0026	0.0019	-1.323	0.1869	-0.0028	0.0019	-1.474	0.1416
	x12*Fx2	-0.0042	0.0029	-1.450	0.1482	-0.0032	0.0029	-1.092	0.2757
	SEX(Fx10)	0.3776	0.2507	1.507	0.1329	0.4084	0.2412	1.694	0.0914
	SMS(Fx11)	-0.2245	0.2368	-0.948	0.3439	-0.2012	0.2293	-0.877	0.3812
AIC	**345.513**					**301.0**			

Table 1: Results for mean and dispersion models for serum creatinine from Gamma & Log-normal fit

Discussion

The mean and variance SCT analysis outputs for Log-normal and Gamma fitted models are shown in Table 1. The SCT fitted Log-normal mean and variance models are shown above. In Table 1, there are some discrepancies in SCT fitting between the Log-normal and Gamma models (Table 1), which are well illustrated in [35].

In the given data set, there are only two heart disease related risk factors such as ejection fraction (EFT) (x5) and high blood pressure status (BP) (0= normal BP, 1=high BP) (Fx6). The data set contains only one anaemia status (ANS) disease factors, (0= no anaemia, 1= anaemia) (Fx2), and only one subject's diabetes mellitus status (0= no diabetes, 1= diabetes) (DMS) (Fx4). Table 1 shows different mean-variance associations of SCT with (i) cardiac parameters (EFT & BP) (ii) anaemia status (ANS) disease factor and (iii) subject's diabetes mellitus status (DMS), and the effects of SCT on the cardiac parameters, anaemia status and diabetes mellitus status are discussed in the following paragraphs.

From the SCT fitted mean Log-normal model (Table 1), it is derived that mean SCT is positively associated with AGE (P<0.0001). It indicates that the mean SCT level increases as the age increases. Mean SCT is partially negatively associated with ejection fraction (EFT) (P=0.0974) and partially positively associated with the joint interaction effects of EFT*DEE (0=alive, 1=death) (P=0.1168). It indicates that SCT level increases as the joint effect EFT*DEE increases. In other words, SCT level is higher for the cardiac patients who are near to death than the surviving cardiac patients. Mean SCT level is negatively associated with high blood pressure (BP) (P=0.0030), indicating that SCT level increases as the BP decreases. It indicates that higher levels of SCT can decrease BP, which may invite stroke for the cardiac patients. SCT variance is negatively associated with EFT (P=0.0019) and ANS (P=0.0044), while it is positively associated with their JIEs of EFT*ANS (P=0.0234).It indicates that SCT level's scatteredness increases for the anaemia patients with higher EFT levels. SCT variance is negatively associated with PLC (P=0.0547) and BP (P=0.0137), while it is positively associated with their JIEs of PLC*BP (P=0.0347). It implies that SCT level's scatteredness increases for the BP patients with higher PLC levels. SCT variance is negatively associated with DEE (P=0.0002) and EFT (P=0.0019), while it is positively associated with their JIEs of EFT*DEE (P<0.0001). This indicates that SCT level's scatteredness increases for the cardiac patients near to death with higher EFT levels.

From the SCT fitted mean Log-normal model (Table 1), it is derived that mean SCT level is partially negatively associated with the JIEs of anaemia status (ANS) (0= no anaemia, 1= anaemia) and time up to the end of the follow-up period (TFP) i.e., ANS*TFP (P=0.1299), while it is independent of both the ANS (P=0.4901) and TFP (P=0.3731). This indicates that the mean SCT level is higher for non-anaemia patients with smaller follow up time. The variance of SCT is negatively associated with age (P=0.0543) and ANS (P=0.0044), while it is positively associated with their JIEs, i.e. AGE*ANS (P=0.0070). It indicates that SCT level's scatteredness increases for the anaemia patients with older ages. SCT variance is negatively associated with CPK (P=0.0001), while it is partially positively associated with the JIEs of CPK and ANS i.e., CPK*ANS (P=0.1482). This implies that SCT level's scatteredness increases for the anaemia patients with higher CPK levels. SCT variance is negatively associated with TFP (P=0.1416) (partially) and ANS (P=0.0044), while it is partially negatively associated with their JIEs of TFP*ANS (P=0.2757). This indicates that SCT level's scatteredness increases for the non-anaemia patients with lower follow up time. Same as cardiac patients, it can be restated that SCT variance is negatively associated with EFT (P=0.0019) and ANS (P=0.0044), while it is positively associated with their JIEs of EFT*ANS (P=0.0234) It indicates that SCT level's scatteredness increases for the anaemia patients with higher EFT levels.

From the SCT fitted mean Log-normal model (Table 1), it is observed that mean SCT is not associated with the subject's diabetes mellitus status (DMS) (0= no diabetes, 1= diabetes), while its variance is associated with DMS. Note that variance of SCT is negatively associated with DMS (P=0.0199) and CPK (P=0.0001), while it is positively associated with their JIEs of CPK*DMS (P=0.0086). It indicates that SCT level's scatteredness increases for the diabetes patients with higher CPK levels.

From the SCT fitted Log-normal model (Table 1), it is observed that mean and variance of SCT are associated with some other factors, which are not jointly associated with the above three disease factors. Note that mean SCT is negatively associated with creatinine phosphokinase (CPK) (P<0.0001) and serum sodium (SNa) (P<0.0001), while it is positively associated with their JIEs, i.e., CPK*SNa (P<0.0001). It indicates that mean SCT level increases as the joint effect of CPK*SNa increases. In addition, mean SCT is negatively associated with the smoking status (SMS) (P=0.0007), and positively associated with the JIEs of SMS and TFP, i.e. SMS*TFP (P=0.0016), while TFP (P=0.3731) is insignificant. It indicates that mean SCT level rises as the joint effect SMS*TFP increases. Also, variance of SCT is partially positively associated SEX (0=female, 1=male) (P=0.0914), it implies that SCT level's scatteredness increases for the male subjects than female.

Conclusions

The report has derived the associations of SCT with cardiac factors EFT & BP, anaemia status, diabetes status and some other physiological and biochemical parameters of some cardiac patients. The fitted SCT models is finalized based on the smallest AIC value on comparison of both Log-normal (AIC=301.0) and Gamma (AIC=345.513) fitted JGLMs, model diagnostic plots (Figure 1) and small standard error of the estimates (Table 1). It has been derived herein that SCT level increases at older ages, and for smokers with the joint effect of long time follow up. In addition, SCT level is higher for the cardiac patients who are near to death than the surviving cardiac patients, and also higher SCT levels can decrease BP, that may invite stroke for the cardiac patients. Also, the mean SCT level is higher for non-anaemia patients with smaller follow up time. Mean SCT level increases as the joint effect of CPK*SNa increases. Moreover, SCT's variance level has different associations of many factors that have been discussed above. The given data set does not give any information regarding kidney patients, so it is not possible to conclude about the kidney patients. The current data set does not contain diabetes markers such as glucose level, HbA1c, anaemia indicator hemoglobin, and many other cardiac parameters. So, the current report is unable to focus on the effects of SCT on these above parameters. It is expected that future researchers may consider these parameters for more fruitful studies. Therefore, the report will help the cardiac, anaemia, diabetes patients, researchers and practitioners to know the effect of SCT

levels. Care should be taken for the SCT levels at older ages along with smoking, SNa and CPK levels.

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